

- d) selecting and cloning transduced cells which have the altered biological function, and
  - e) performing one, or both, of
    - i) isolating and sequencing vector DNA in the cells having the altered biological function, and deducing, from the sequenced vector DNA, the sequence of the ribonucleic acid, thereby, identifying the biologically active ribonucleic acid, and
    - ii) isolating the ribonucleic acid in the cells having the altered biological function and using the isolated ribonucleic acid, directly, to select a ligand molecule to the ribonucleic from a peptide library, thereby, identifying the cellular ligand to the biologically active ribonucleic acid.
119. The method according to claim 118, in which the synthetic totally random DNA sequences are produced by random oligonucleotide synthesis.
120. The method according to claim 118, in which the synthetic totally random DNA sequence is introduced into vectors by site directed polymerase chain reaction-mediated mutagenesis thereby ensuring complexity of the totally random DNA sequences.
121. The method according to claim 120, in which the site directed polymerase chain reaction-mediated mutagenesis produces reaction products having 3' ends, and the 3' ends are trimmed from the reaction products with a 3'-5' exonuclease.
122. The method according to claim 118, in which the step of producing the pool of expression vectors comprises ligating a DNA fragment into a vector in an optimized manner by performing temperature cycling ligation and, thereby, maintaining a high diversity of the totally random DNA sequences for transfection into packaging cells.
123. The method according to claim 118, in which the appropriate viral vector is selected from the group consisting of a retrovirus vector and a vaccinia virus vector.
124. The method according to claim 123, in which the appropriate viral vector is the retroviral vector.
125. The method according to claim 124, in which the retroviral vector has heterologous ends to facilitate polymerase chain reaction-based generation of the synthetic totally random DNA sequences.

126. The method according to claim 125, in which the heterologous ends contain two different promoters.
127. The method according to claim 124, in which the retroviral vector has a 5'-LTR containing a CMV promoter in place of a viral promoter.
128. The method according to claim 123, in which the synthetic totally random DNA sequences are linear polymerase chain reaction products directly introduced into virus packaging cells by non-viral transfection methods.
129. The method according to claim 123, in which viral vector DNA introduced into the cells is amplified directly by polymerase chain reaction followed by transfection of further cells with amplified vector DNA with the purpose of eliminating false positives, or enabling the "one cell - one ribonucleic acid" concept, or eliminating false positives and enabling the "one cell - one ribonucleic acid" concept.
130. The method according to claim 123, wherein the expression vectors are produced by a packaging cell line, wherein the packaging cell line is transfected under transient conditions with a functional tRNA gene corresponding to a primer binding site (PBS) in the appropriate viral vector thereby increasing production of the expression vectors by the packaging cell line.
131. The method according to claim 123, wherein the appropriate viral vector is produced by a semi-packaging cell line transfected with a suitable minivirus/vector thereby enabling vector expression after transduction of cells rather than after transfection of cells.
132. The method according to claim 118, wherein the altered biological function is up-regulation or down-regulation of expression of a cell surface protein.
133. The method according to claim 123, wherein the appropriate viral vector is the vaccinia virus vector.
134. In a drug development method, wherein a lead compound serves as starting point for design and synthesis of candidate drugs, the improvement wherein the lead compound is the biologically active ribonucleic acid identified by the method according to claim 118.

135. The method according to claim 118, wherein the biologically active ribonucleic acid is used directly for isolation of a cellular target protein to the ribonucleic acid present in the transduced cells.
136. The method according to claim 118, wherein the identical eukaryotic cells are mammalian.
137. The method according to claim 118, wherein the identical eukaryotic cells are cells of a cell clone or a cell line.
138. The method according to claim 118, wherein the synthetic totally random DNA sequences are coupled to or inserted into the coding sequence of a protein.
139. A method for identification of biologically active ribonucleic acids or cellular ligands to the biologically active ribonucleic acids, which comprises the steps of
- a) producing a pool of appropriate vectors each containing a synthetic totally random DNA sequence to be examined,
  - b) efficiently transducing the vectors into a number of identical eukaryotic cells in such a way that each cell expresses a single ribonucleic acid encoded by the DNA sequence to be examined or a limited number of different ribonucleic acids encoded by DNA sequences to be examined,
  - c) screening the transduced cells to see whether some of them exhibit up-regulation or down-regulation of a preselected cellular function, and
  - d) selecting and cloning cells which have up-regulated or down-regulated the preselected cellular function,
  - e) performing one, or both, of
    - i) isolating and sequencing the vector DNA in the cloned cells exhibiting up-regulation or down-regulation of the preselected cellular function, and deducing, from the sequenced vector DNA, the sequence of the ribonucleic acid, thereby, identifying the biologically active ribonucleic acid, and
    - ii) isolating the ribonucleic acid in the cells exhibiting up-regulation or down-regulation of the preselected cellular function, and using the isolated ribonucleic acid, directly, to select a ligand molecule to the ribonucleic acid